

CLAIMS

1. (Cancelled). A method of altering the immunoreactivity of human cells, which method comprising introducing a gene encoding an accessory molecule ligand into said cells so that said accessory molecule ligand is expressed on the surface of said cells.
2. (Cancelled). The method of claim 1 wherein the accessory molecule to which the accessory molecule ligand specifically binds is also present on the surface of said human cells.
3. (Cancelled). The method of claim 1 wherein said human cells are neoplastic human cells.
4. (Cancelled). The method of claim 1 wherein said accessory molecule ligand gene is a chimeric gene.
5. (Cancelled). The method in claim 1 wherein said accessory molecule ligand gene is present in a vector capable of transducing human cells.
6. (Cancelled). The method of claim 1 wherein said accessory molecule ligand gene is present as part of a genetic vector.
7. (Cancelled). The method of claim 1 wherein said accessory molecule ligand gene is operatively linked to a promoter region and a polyadenylation signal.
8. (Cancelled). The method of claim 1 wherein said gene is a CD40 ligand gene.
9. (Cancelled). The method of claim 7 wherein said CD40 ligand gene is a murine CD40 ligand gene.
10. (Cancelled). The method of claim 4 wherein said gene is a chimeric gene which comprises at least a portion of a murine CD40 ligand gene.
11. (Withdrawn). A method of treating a human neoplasia comprising inserting into said human neoplastic cells a gene which encodes an accessory molecule ligand into said human neoplastic cells so that said accessory molecule ligand is expressed on the surface of said neoplastic cells.
12. (Withdrawn). The method of claim 11 further comprising:
 - a) obtaining said human neoplastic cells from a human patient;
 - b) infusing said human neoplastic cells after having inserted said accessory molecule ligand on the surface of said cells back into said patient.

13. (Withdrawn). The method of claim 11 wherein the accessory molecule to which the said accessory molecule ligand specifically binds is present on the surface of said human neoplastic cells.
14. (Withdrawn). The method of claim 11 wherein said accessory molecule ligand gene is a chimeric gene.
15. (Withdrawn). The method of claim 11 wherein said accessory molecule ligand gene is a chimeric gene which contains at least a portion of the murine CD40 ligand gene.
16. (Withdrawn). The method of claim 11 wherein said accessory molecule ligand gene is present as part of a genetic vector.
17. (Withdrawn). The method of claim 11 wherein said accessory molecule ligand gene is operatively linked to a promoter region and a 3' end region.
18. (Withdrawn). The method of claim 11 wherein said accessory molecule ligand gene is a CD40 ligand gene.
19. (Withdrawn). The method of claim 11 wherein the said CD40 ligand gene is a murine CD40 ligand gene.
20. (Withdrawn). The method of claim 11 wherein said accessory molecule ligand gene is a Fas-ligand gene or a CD27 ligand gene.
21. (Withdrawn). The method of claim 11 wherein said accessory molecule ligand gene is present in a gene therapy vector.
22. (Withdrawn). A method of treating a neoplasia in a patient comprising injecting into the tumor bed of said patient a gene which encodes an accessory molecule ligand so that said accessory molecule ligand is expressed on the surface of said tumor cells thereby causing said cells to participate in an immune reaction.
23. (Withdrawn). A gene therapy vector containing an accessory molecule ligand gene.
24. (Withdrawn). The gene therapy vector of claim 23 wherein said accessory molecule gene is a CD40 ligand gene.
25. (Withdrawn). The gene therapy vector of claim 23 wherein said CD40 ligand gene is a murine CD40 ligand gene.
26. (Withdrawn). The gene therapy vector of claim 23 wherein said CD40 ligand gene is a chimeric gene.
27. (Withdrawn). The gene therapy vector of claim 23 wherein said chimeric gene contains at least a portion of the murine CD40 ligand gene.

28. (Withdrawn). The gene therapy vector of claim 23 wherein at least a portion of said vector is derived from adenovirus DNA.
29. (Withdrawn). The gene therapy vector of claim 23 wherein said vector contains at least a promoter region and a 3' end region.
30. (Withdrawn). The gene therapy vector of claim 23 wherein said promoter region and said 3' end region are not derived from the same species from which the CD40 ligand gene is derived.
31. (Withdrawn). The gene therapy vector of claim 23 wherein said portion of said vector is derived from viral DNA.
32. (Withdrawn). The gene therapy vector of claim 23 wherein at least a portion of said vector is derived from a retrovirus.
33. (Withdrawn). The gene therapy vector of claim 23 wherein said vector is capable of transducing human cells.
34. (Withdrawn). The gene therapy vector of claim 23 wherein said vector is capable of transducing animal cells.
35. (Withdrawn). The gene therapy vector of claim 23 wherein said human cells are human neoplastic cells.
36. (Withdrawn). The gene therapy vector of claim 23 wherein said human cells are human antigen presenting cells.
37. (Withdrawn). A genetic construct containing a promoter operatively linked to an accessory molecule ligand gene which is also operatively linked to a polyadenylation signal.
38. (Withdrawn). A genetic construct in which a promoter is operatively linked to a chimeric accessory molecule ligand gene and a polyadenylation signal.
39. (Withdrawn). A gene therapy vector containing a chimeric accessory molecule ligand gene.
40. (Withdrawn). The gene therapy vector of claim 39 wherein said chimeric accessory molecule ligand gene contains at least one gene segment derived from a murine CD40 ligand gene and other gene segments derived from other accessory molecule genes.
41. (Withdrawn). The gene therapy vector of claim 39 wherein said other accessory molecule ligand genes are human accessory molecule ligand genes.

42. (Withdrawn). The gene therapy vector of claim 39 wherein said human accessory molecule ligand genes are human CD40 ligand genes.
43. (Withdrawn). A human cell containing the gene therapy vector of claims 23-36 or 39-42 or the genetic construct of claims 37-38.
44. (Withdrawn). The human cell of claim 43 wherein said cell is an antigen presenting cell.
45. (Withdrawn). The human cell of claim 43 wherein said human cell is a neoplastic cell.
46. (Withdrawn). The human cell of claim 43 wherein said cell is an accessory cell.
47. (Withdrawn). An animal cell containing the gene therapy vector or genetic construct of claims 23-43.
48. (Withdrawn). An insect cell containing the gene therapy vector or genetic construct of claims 23-43.
49. (Withdrawn). A bacterial cell containing the gene therapy vector or genetic construct of claims 23-43.
50. (Withdrawn). A method of vaccinating an animal against a predetermined organism comprising: administering into an animal to be immunized against a predetermined organism, a vaccine comprising immunogenic antigens capable of causing an immune response to said predetermined organism together with a vector containing a gene including an accessory molecule ligand.
51. (Withdrawn). The method of claim 50 wherein said immunogenic antigens are encoded by genes present on a genetic vector.
52. (Withdrawn). The method of claim 50 wherein said gene is a chimeric gene.
53. (Withdrawn). The method of claim 50 wherein said chimeric gene contains at least a portion of a murine CD40 ligand gene.
54. (Withdrawn). The method of claim 50 wherein said chimeric gene contains at least a segment of a murine CD40 ligand gene and at least a segment of a different accessory molecule gene.
55. (Withdrawn). The method of claim 50 wherein said predetermined organism is a virus, a bacteria, a fungus or a neoplastic cell.
56. (Withdrawn). A method of producing an immune response directed to a predetermined antigen comprising: administering to said animal a genetic vector containing a gene encoding the

antigen to which said immune response is desired together with a genetic vector containing a gene encoding an accessory molecule ligand gene.

57. (Withdrawn). A chimeric accessory molecule ligand gene comprising at least one domain or sub-domain gene segment derived from a first accessory molecule ligand gene operatively linked to the domain or sub-domain gene segment of a second accessory molecule ligand gene.

58. (Withdrawn). The chimeric accessory molecule ligand gene of claim 57 in which said first and second accessory molecule ligand genes are selected from the group consisting of the genes from any species encoding a member of the tumor necrosis family, CD40-ligand, Fas-ligand, CD70, TNF α , TNF β , CD30 ligand, 4-1 BB ligand (4-1 BBL), TNF-related apoptosis inducing ligand (TRAIL) and nerve growth factor.

59. (Withdrawn). The chimeric accessory molecule ligand gene of claim 57 in which at least one of said domain or sub-domain gene segments is an artificial gene segment.

60. (Withdrawn). The chimeric accessory molecule encoded by the genes of claims 57-59.

61. (Withdrawn). A chimeric accessory molecule ligand gene comprising at least a portion of the gene encoding Domains I and II derived from an accessory molecule ligand operatively linked to at least a portion of the gene encoding a Domain of an accessory molecule ligand which in turn is operatively linked to at least a portion of the gene encoding Domain IV of an accessory molecule ligand.

62. (Withdrawn). The chimeric accessory molecule ligand gene of claim 61 wherein said Domains I and II are derived from the human CD40 ligand gene.

63. (Withdrawn). The chimeric accessory molecule ligand gene of claim 61 wherein said Domain is the human Fas-ligand Domain IV.

64. (Withdrawn). The chimeric accessory molecule ligand gene of claim 61 wherein said Domain is Domain III of another accessory molecule ligand.

65. (Withdrawn). The chimeric accessory molecule ligand gene of claim 61 wherein said Domain is a domain from the same accessory molecule ligand.

66. (Withdrawn). The chimeric accessory molecule ligand gene of claim 61 wherein said Domain is an artificial domain.

67. (Cancelled). The method of claim 4 wherein said chimeric gene is a gene of claims 57-60.

68. (Withdrawn). The method of claim 11 wherein said accessory molecule ligand gene is a chimeric accessory molecule ligand gene of claims 57-60.

69. (Withdrawn). The gene therapy vector of claim 23 wherein said chimeric gene is a chimeric accessory molecule ligand gene of claims 57-60.

70. (Withdrawn). A method of treating rheumatoid arthritis in a joint comprising inserting into the joint a vector containing a gene which encodes an accessory molecule ligand so that said accessory molecule ligand is expressed on the surface of cells within the joint.

71. (Withdrawn). The method of claim 70 wherein said accessory molecule ligand gene is a chimeric accessory molecule ligand gene which is comprised of at least a portion of a human Fas-ligand gene.

72. (Withdrawn). The method of claim 70 wherein said accessory molecule ligand gene is a chimeric accessory molecule ligand gene which contains at least a portion of the murine Fas-ligand gene.

73. (Withdrawn). The method of claim 70 wherein said accessory molecule ligand gene is a murine Fas-ligand gene.

74. (Withdrawn). The method of claim 70 wherein said accessory molecule ligand gene is the murine Fas-ligand gene.

75. (Withdrawn). The method of claim 70 wherein said accessory molecule ligand gene is a chimeric accessory molecule gene comprised of at least a portion of domain III from the murine Fas-ligand gene and a portion of domain IV from the human Fas-ligand gene.

76. (Withdrawn). The method of claim 70 wherein said accessory molecule ligand gene is a chimeric accessory molecule ligand gene comprised of a portion of domain III of the human CD70 gene and at least a portion of domain IV of the human Fas-ligand gene.

77. (Withdrawn). A method of treating rheumatoid arthritis in a joint comprising inserting into the joint cells which have been transformed with a gene which encodes an accessory molecule ligand which is expressed on the surface of said cells.

78. (Withdrawn). A chimeric accessory molecule ligand comprised of at least a portion of the fourth domain of human Fas-ligand.

79. (Withdrawn). A chimeric accessory molecule ligand derived from a Fas-ligand in which at least one matrix metalloproteinase cleavage site has been removed.

80. (Withdrawn). A chimeric accessory molecule ligand comprised of domain III of the Murine Fas-ligand or the human CD70 gene, and domain IV of the human Fas-ligand.

81. (Withdrawn). A gene therapy vector containing a gene encoding chimeric accessory molecule of claims 78-80.

82. (Withdrawn). A cell containing a gene therapy vector of claim 81.

83. (Cancelled). A method of altering the immunoreactivity of human cells, which method comprising introducing a gene encoding an accessory molecule ligand which has a stabilized activity into said cells so that said accessory molecule ligand is expressed on the surface of said cells.

84. (Cancelled). The method of claim 1 wherein said chimeric accessory molecule ligand gene comprises at least one domain or sub-domain gene segment derived from a first accessory molecule ligand gene operatively linked to the domain or sub-domain gene segment of a second accessory molecule ligand gene.

85. (Cancelled). The method of claim 84 wherein said first and second accessory molecule ligand genes are selected from the group consisting of the genes from any species encoding CD40-ligand, Fas-ligand, CD70, TNF_a, TNF_b, CD30 ligand, 4-1 BB ligand (4-1 BBL), TNF-related apoptosis inducing ligand (TRAIL) and nerve growth factor.

86. (Cancelled). The method of claim 84 wherein at least one of said domain or sub-domain gene segments is an artificial gene segment.

87. (Amended). A method for expressing a chimeric CD40 ligand in a CD40+ human cell, wherein the chimeric CD40 ligand includes one or more human domains derived from a human CD40 ligand gene and one or more mouse domains derived from a mouse CD40 ligand gene, the method comprising introducing a chimeric polynucleotide encoding the chimeric CD40 ligand into the cell.

88. (Cancelled). The method of claim 87 wherein the non-human CD40 ligand comprises murine CD40 ligand.

89. (Cancelled). A method for expressing a ligand capable of binding to a CD40 ligand receptor in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or subdomain of human CD40 ligand and a domain or subdomain of non-human CD40 ligand into the cell.

90. (Cancelled). A method for increasing the concentration of a ligand on the surface of a human cell, wherein the ligand is capable of binding to a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or subdomain of human CD40 ligand and a domain or subdomain of non-human CD40 ligand into the human cell, wherein the encoded CD40 ligand has increased stability on the surface of the cell relative to that of a human CD40 ligand.

91. (Cancelled). The method of claims 89 and 90 wherein the chimeric CD40 ligand comprises one or more human CD40 ligand domain or subdomain and one or more non-human CD40 ligand domain or subdomain.

92. (Cancelled). The method of claim 89 or 90, wherein the non-human CD40 ligand domain or subdomain comprises a murine CD40 ligand domain or subdomain.

93. (Amended). The method of claim 87 wherein the mouse domain comprises an extracellular CD40 ligand domain.

94. (Amended). The method of claim 87 wherein the mouse CD40 ligand domain comprises Domain III of the mouse CD 40 ligand.

95. (Amended). The method of claim 93 wherein the extracellular domain consists of Domain IV.

96. (Cancelled). The method of claim 94 wherein the murine CD40 ligand further comprises Domain IV, or a subdomain of Domain IV, of the murine CD40 ligand.

97. (Amended). The method of claim 87 wherein the mouse CD 40 ligand consists of Domain I of the mouse CD40 ligand.

98. (Amended). The method of claim 87 wherein the mouse CD40 ligand consists of Domain II of the mouse CD40 ligand.

99. (Amended). The method of claim 87 wherein the chimeric polynucleotide consists of the nucleic acid sequence of SEQ ID NO. 3.

100. (Amended). The method of claim 87 wherein the chimeric polynucleotide consists of the nucleic acid sequence of SEQ ID NO. 20.

101. (Cancelled). The method of claims 89 or 90, wherein the introduction of the nucleic acid sequence into the cell results in induced expression of surface markers on the cell.

102. (Cancelled). The method of claim 101, wherein the surface markers comprise CD54, CD80, CD86, CD58, CD70, or CD95.

103. (Cancelled). A method for expressing a ligand capable of binding to a CD40 ligand receptor in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or subdomain of human CD40 ligand and a domain or subdomain of a non-human ligand selected from the group consisting of CD40 ligand, TNF-alpha, TNF-beta, CD70, CD30 ligand, 4-1 BBL, nerve growth factor and TNF-related apoptosis inducing ligand (TRAIL).

104. (Cancelled). The method of claim 103 or claim 137, wherein the non-human ligand domain or subdomain comprises a murine ligand domain or subdomain.

105. (Cancelled). The method of claim 104 wherein the murine ligand comprises Domain III, or a subdomain of Domain III, or the murine ligand.

106. (Cancelled). The method of claim 104 wherein the murine ligand comprises Domain IV, or a subdomain of Domain IV, of the murine ligand.

107. (Cancelled). The method of claim 105 wherein the murine ligand further comprises Domain IV, or a subdomain of Domain IV, of the murine ligand.

108. (Cancelled). A method for expressing a ligand capable of binding to a CD40 ligand receptor in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or subdomain of human CD40 ligand and a domain or subdomain of a human ligand selected from the group consisting of CD40 ligand, TNF-alpha, TNF-beta, CD70, CD30 ligand, 4-1 BBL, nerve growth factor and TNF-related apoptosis inducing ligand (TRAIL).

109. (Cancelled). The method of claim 108 or 138, wherein the human CD40 ligand comprises Domain IV, or a subdomain of Domain IV, of human CD40 ligand.

110. (Cancelled). The method of claim 109 wherein the chimerical CD40 ligand comprises Domains I, II, and IV of human CD40 and Domain III of human CD70 receptor ligand.

111. (Thrice Amended). The method of claim 87, wherein the human CD40+ cell comprises a neoplastic cell.

112. (Cancelled). The method of claims 89 and 90 wherein the cell comprises a cell from connective tissue surrounding neoplastic cells.

113. (Amended). The method of claim 111, wherein the neoplastic cell comprises a neoplastic B cell.

114. (Cancelled). The method of claim 113, wherein the neoplastic B cell comprises a CLL cell.

115. (Cancelled). The method of claim 113 wherein the neoplastic B cell is derived from a patient with a B cell malignancy.

116. (Amended). The method of claim 111 wherein the neoplastic cell comprises a neoplastic T cell.

117. (Cancelled). The method of claim 111 wherein the neoplastic cell comprises a dendritic cell.

118. (Cancelled). The method of claim 111 wherein the neoplastic cell comprises a monocyte.

119. (Cancelled). The method of claim 111 wherein the neoplastic cell comprises a myelomonocyte.

120. (Cancelled). The method of claim 111 wherein the neoplastic cell comprises a cell derived from a breast tumor.

121. (Cancelled). The method of claim 111 wherein the neoplastic cell comprises a cell derived from an ovarian tumor.
122. (Cancelled). The method of claim 111 wherein the neoplastic cell comprises a cell derived from a lung tumor.
123. (Cancelled). A method for expressing a ligand capable of binding to a CD40 ligand receptor in a human neoplastic cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a chimeric CD40 ligand into the cell.
124. (Cancelled). A method for increasing the concentration of a ligand on the surface of a human neoplastic cell, wherein the ligand is capable of binding to a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a chimeric CD40 ligand into the human cell, the chimeric CD40 ligand having increased stability on the surface of the cell relative to that of a human CD40 ligand.
125. (Cancelled). The method of claims 123 and 124, wherein the neoplastic cell comprises a neoplastic B cell.
126. (Cancelled). The method of claim 125, wherein the neoplastic B cell comprises a CLL cell.
127. (Cancelled). The method of claim 125 wherein the neoplastic B cell is derived from a patient with a B cell malignancy.
128. (Cancelled). The method of claims 123 and 124, wherein the neoplastic cell comprises a neoplastic T cell.
129. (Cancelled). The method of claims 123 and 124 wherein the neoplastic cell comprises a dendritic cell.
130. (Cancelled). The method of claims 123 and 124 wherein the neoplastic cell comprises a monocyte.
131. (Cancelled). The method of claims 123 and 124 wherein the neoplastic cell comprises a myelomonocyte.
132. (Cancelled). The method of claims 123 and 124 wherein the neoplastic cell comprises a cell derived from a breast tumor.
133. (Cancelled). The method of claims 123 and 124 wherein the neoplastic cell comprises a cell derived from an ovarian tumor.
134. (Cancelled). The method of claims 123 and 124 wherein the neoplastic cell comprises a cell derived from a lung tumor.

135. (Cancelled). A method for expressing a ligand capable of binding to a CD40 ligand receptor in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a chimeric CD40 ligand into the cell, wherein the cell is derived from connective tissue surrounding neoplastic cells.

136. (Cancelled). A method for increasing the concentration of a ligand on the surface of a human cell derived from connective tissue surrounding neoplastic cells, wherein the ligand is capable of binding to a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a chimeric CD40 ligand into the human cell, the chimeric CD40 ligand having increased stability on the surface of the cell relative to that of a human CD40 ligand.

137. (Cancelled). A method for increasing the concentration of a ligand on the surface of a human cell, wherein the ligand is capable of binding to a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or sub-domain of human CD40 ligand and a non-human ligand selected from the group consisting of CD40 ligand, TNF-alpha, TNF-beta, CD70, CD30 ligand, 4-1 BBL, nerve growth factor and TNF-related apoptosis inducing ligand (TRAIL).

138. (Cancelled). A method for increasing the concentration of a ligand on the surface of a human cell, wherein the ligand is capable of binding to a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or sub-domain of human CD40 ligand and a human ligand selected from the group consisting of CD40 ligand, TNF-alpha, TNF-beta, CD70, CD30 ligand, 4-1 BBL, nerve growth factor and TNF-related apoptosis inducing ligand (TRAIL).

139. (Cancelled). The method of claims 89, 90, 103, 108, 137, or 138, wherein the cell comprises a human non-neoplastic cell that is CD40+.

140 (Cancelled). The method of claim 139, wherein the cell comprises a B cell.

141. (Previously Presented) The method of claim 87 wherein the chimeric polynucleotide consists of the nucleic acid sequence of SEQ ID NO. 4.

142. (Previously Presented) The method of claim 87 wherein the chimeric polynucleotide consists of the nucleic acid sequence of SEQ ID NO. 5.

143. (Previously Presented) The method of claim 87 wherein the chimeric polynucleotide consists of the nucleic acid sequence of SEQ ID NO. 6.

144. (Previously Presented) The method of claim 87 wherein the chimeric polynucleotide consists of the nucleic acid sequence of SEQ ID NO. 7.